

## **REMARKS**

In response to the Office Action mailed December 14, 2006, Claims 1-3, 8, 9, 11-12 stand rejected. Claims 11 and 12 are cancelled. Claims 1-3, 8, and 9 are thus pending.

### **I. Priority Date**

Applicant shall file a certified copy of foreign priority application 03013471.2 EPO, now published as WO 2005/000362 A1. A copy of said publication was filed as part of Applicant's PCT submittal on December 20, 2005. The WO '362 publication clearly references, under the heading "Priority Data", the foreign priority application EP 03013471.2 with a foreign priority date of June 25, 2003.

### **II. Information Disclosure Statement**

Applicants have corrected the typographical error regarding dates in the March 14, 2006 IDS submission. A corrected form 1449 reflecting same, and the author for reference C4, is hereby attached to this response. Applicant respectfully notes that titles of the publications for C1-C9 were submitted in the March 14, 2006 IDS submission. Applicant respectfully submits that the IDS submittal is therefore in compliance with 37 CFR 1.97 et seq.

### **III. Claim Rejections**

#### **A. 35 USC 112**

Claims 11-12 stand rejected by the Examiner under 35 USC 112 first and second paragraphs for alleged lack of written description and for indefiniteness. Applicant has cancelled claims 11-12 and therefore submits that the rejection is now obviated.

#### **B. 35 USC 102**

Claims 1-3, 8, 9 and 11-12 stand rejected by the Examiner under 35 USC 102 as being anticipated by Dean et al. (WO 97/22367). Applicants respectfully traverse.

Dean is alleged to teach a sulfur-isotope (S-35) radiolabeled growth hormone secretagogue of MK0677 methanesulfonate salt. The Examiner acknowledges that Dean does not disclose nor teach a tritium labeled growth hormone secretagogue. The Examiner alleges however that the sulfur-isotope labeled secretagogue would inherently contain some tritium at some locale on the secretagogue in place of a hydrogen atom and as such said tritium would be eventually found in one of the methyl groups (but nowhere else) in the S-35 radiolabelled secretagogue of Dean. Applicants respectfully traverse and overcome said rejection.

Applicants' claim concerns a tritiated-labelled growth hormone secretagogue of Formula I, wherein said radiolabelling is limited to one to six specific hydrogens as in Formula I. Applicant does not claim radiolabelling of any other atom besides that of one to six specific hydrogens at specific locations on said secretagogue. Applicant does not claim radiolabelling of the sulfur atom. As such, Dean does not anticipate Applicant's invention as Dean requires the presence of the S-35 (sulfur-isotope) and does not require the presence of tritium.

Furthermore, Dean actually teaches away from Applicant's invention. As noted on page 3, line 31 through page 4, line 8, Dean states that "[p]revious attempts to develop a binding assay using [3H] labeled ... peptide ligands derived from GHRP-6 met with limited success (citations omitted)" and that "[g]enerally, the binding of such peptide ligands was of low affinity and of excessively high capacity [and] [m]oreover, the binding affinities (especially of tritium labeled GHRP-6) did not correlate with the growth hormone secretory activity of the peptides" (emphasis added). Thus, Dean teaches that one should use S-35 and not tritium in labelling growth hormone secretagogues. Thus, by following Dean, one would ensure that no H was replaced by a hydrogen isotope, especially tritium. As tritium comprises at best about one billionth of one billionth of a percent of natural hydrogen (or comprises 0.0000000000000001 % of natural hydrogen or  $10^{-16}$  %, see attached article from the Argonne National Laboratory),

Dean's teaching to use S-35 as opposed to tritium in labelling growth hormone secretagogues would preclude tritium being present in Dean's taught S-35 radiolabelled secretagogue.

As Dean therefore teaches away from Applicant's claimed invention, Applicants respectfully submit the 102(b) rejection hereby is overcome and respectfully request that Claims 1-3, 8 and 9 be placed into condition for allowance.

C. 35 USC 103(a)

1. Claims 1-3, 8, 9 and 11-12 stand rejected by the Examiner under 35 USC 103(a) as being unpatentable over Jones et al (J. Labelled Compounds and Radiopharm. 1996, 38, 561-565) in view of Dean et al. (WO 97/22367). Applicants respectfully traverse.

Jones is alleged to teach carbon-14 radiolabelled growth hormone secretagogue MK0677 and that dilute solutions/batches of tritium labeled tracer were prepared with high specific activity. The Examiner acknowledges that Jones fails to disclose or teach methods of identifying a cellular receptor as a growth hormone receptor, nor does Jones teach a method for identifying a compound that can bind to a growth hormone secretagogue receptor. Applicants respectfully traverse and overcome said rejection.

As acknowledged by the Examiner, Jones fails to teach the specific location of the tritium labelling on the growth hormone secretagogue. However, the Examiner fails to recognize the teaching away in Dean from tritium labelling growth hormone secretagogues. As discussed ante, Dean states that "the binding affinities (especially of tritium labeled GHRP-6) did not correlate with the growth hormone secretory activity of the peptides" (emphasis added). Therefore, Dean teaches away from tritium labeling of growth hormone secretagogues. There would thus be no motivation to combine Dean with Jones. There would thus also be no motivation to locate specific sites for tritium labelling, since Dean teaches away from the use of any tritium labelling in growth

hormone secretagogues. Accordingly, the combination of Dean and Jones would not teach Applicant's claimed invention and methods.

As Dean therefore teaches away from Applicant's claimed invention, the combination of Dean and Jones would not teach nor disclose Applicants' claimed invention and methods. Applicants respectfully submit the 103(a) rejection hereby is overcome and respectfully request that Claims 1-3, 8 and 9 be placed into condition for allowance.

2. Claims 1-3, 8, 9 and 11-12 stand rejected by the Examiner under 35 USC 103(a) as being unpatentable over Hakkinen (US 6,548,501). Applicants respectfully traverse.

Hakkinen is asserted to disclose a tritiated growth hormone secretagogue of MK0677. The Examiner acknowledges that Hakkinen fails to teach specific tritiated labelling on one or more of the specific methyl positions of Applicant's claimed compound. Applicant respectfully traverse and overcome said rejection.

Contrary to the Examiner's assertion, Hakkinen merely discloses a generic growth hormone secretagogue compound of formula I which may have one or more of its atoms replaced by an isotope such as deuterium, tritium, carbon-13, carbon-14, nitrogen-15, oxygen-17, oxygen-18, phosphorous-31, phosphorus-32, sulfur-35, fluorine-18 and chlorine-36. Hakkinen does not disclose nor teach the tritium isotope of MK0677, much less does it teach or disclose the precise locations of such isotope atom replacement on the specific secretagogue of Applicant's invention. At best, Hakkinen teaches that in only a few certain undisclosed compounds, deuterium, tritium and carbon-14 may be preferred. Hakkinen does not disclose, nor teach, which certain isotopically labelled compounds would be useful in binding assays etc. Indeed, in the light of Dean et al's teaching that previous attempts to develop tritium-labelled peptide ligands derived from GHRP-6 (a growth hormone releasing peptide) met with at best


limited success, it is readily apparent that said labelling is not predictable at all and may further result in "binding activities (that) did not correlate with the growth hormone secretory activity" (Dean et al). In fact, Hakkinen incorporates the teaching of Dean (Col 22 lines 15-37, incorporating by reference...WO 97/22367).

Accordingly, Applicants respectfully submit that Hakkinen does not teach nor disclose Applicants' claimed invention and as such, Applicants respectfully request that the 103(a) rejection be withdrawn and that Claims 1-3, 8 and 9 be hereby placed into condition for allowance.

As previously noted, Applicants have also attached a revised Form 1449 for the Information Disclosure Statement mailed on March 10, 2006. The information relating to Non Patent Literature has been revised to correct certain typographical errors. The IDS is in conformance with 37 CFR 1.97, 1.98 et seq.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

  
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